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EDITORIAL.

THE MEDICAL MACHINE.

Standardization has become the problem of the modern world. Consequently, as a topic, it has weathered the newspaper correspondence columns, the magazine special articles, and the economics texts. Welcome to the Medical Journal!

On the American continent where is seen the most impressive demonstration of this standardization there has been a concurrent standardization of educational methods to the point where every possible mechanical medium is used for the dissemination of knowledge. In other words, though releasing more time to everyone, mechanical developments have come to dominate the pattern of at least the average intellect and therefore to standardize the methods of education. Despite this, the university remains the outstanding medium for acquiring special knowledge, though all but its professional courses are threatened with extinction because there are no laws requiring a license to practise non-professional knowledge.

In the university, since degrees have no value per se, the Arts student may ignore his course or its method of instruction without serious loss of time or money; but the professional student, should he ignore his course or its method of instruction, must lose considerable time and money, and count those years of study practically wasted. Furthermore, his knowledge is of very little practical value even at the end of the five years and, if it were, he has no license to practise this knowledge.

In professional faculties, this demand for license to practise is unques-

tionably the most important factor governing the teaching system. It stamps the course in a fixed mold prescribed by our educational masters. The effects of this mold may be visualized in the allegory of "The Quest for the Holy License." "Imagine a dun coloured landscape dimly revealing huge boulders against thunderclouds, in the foreground, and in the distance to one side a very small dwelling giving out a faint glimmer of light. Plodding students wander between and over the boulders. Here and there a few figures drop, some behind the 'Anatomical' boulders, more behind the 'Physiological' boulders, and farther in the distance weary ones kneel before the 'Pathological' boulders. As they go on, the clouds of 'Attendance' roll menacingly, for the light is near. And those who have reached the dwelling are forlorn: the Journey has just begun. Success is theirs—at a price!"

It is surprising that, at graduation, even a few students are free from mental apnea: all through the course the so-called Fundamental Sciences are presented with very little demonstration of the fundamentals; all through the course the time is governed completely with little, if any, provision for mental recreation; all through the course they must attend *so many* lectures and "put in" *so many* laboratory periods, though they learn little and that little be forgotten as they face fresh subjects the following years; all through the course they become more and more the academic machine, taking their lectures word for word, copying their laboratory results from previously copied results, and preparing for the almighty examinations by extensive synopses.

Claude Bernard once said of a University that it had fulfilled its duty when it had stimulated its students with a thirst for knowledge. Association with a large number of our graduates will reveal the stark failure of our courses. What Moderns student reads French for the pleasure of its literature? What classics student steeps himself in Homer? What Medical student reads but for his examinations — and license? They toil but they thirst not!

And they thirst not because they are water-logged in details. Prophylaxis for this condition is simple: adapt the intake to the needs of the individual. Such is the essence of the grade plan suggested here. In this plan each student selects one of three grades of each subject in the fundamental sciences. The first grade will include those students thirsting for knowledge: the second grade will include those students desiring details of clinical significance: and the third grade will include those students desiring the essentials only.

Such a plan would make possible for the third grade a reduction in the time of the first four years to about two years which in turn would give the students, those who are feeling their way, opportunity to stop the course without undue loss of money or time. Such a plan would provide for the second grade students, those less gifted in Physics, Chemistry, and Mathematics. Such a plan would give the first grade students opportunities of research and individual teaching. Furthermore, such a plan would not only save time and money but provide opportunity for recreation and interests in Art.

For the teacher this plan might appear cumbersome and time-consuming but reasonable consideration would probably show that it would be simpler, time-saving, and that contact with a small group of interested students would certainly be more enjoyable than the doubtful teaching of a heterogeneous collection.

Our political administrators might question this plan on the point that it is the duty of the university to present a complete knowledge of each subject and that it is the duty of the teachers to inspire the students by their personalities and intellectual appeals. But be-

fore inspiration there must be student enthusiasm and before inspiring there must be professorial enthusiasm. If the student have selection of his course he must have enthusiasm, and if the professor have a minimum of mass teaching of uninterested students and a maximum of individual teaching of interested students he must have enthusiasm.

Alas! Mechanical media cannot displace our professional courses and there is little hope for internal improvement.

Enthusiasm, Curiosity, and License! The greatest of these is License.

Surgery of the Autonomic Nervous System.

By A. D. IRVINE, B.A., 3T1.

Historical.

The history of surgery of the Autonomic Nervous System goes back only a few decades, being of necessity younger than the anatomical and physiological knowledge on which its rationale should be based.

We are now in the second wave of enthusiasm which has followed the original observations of Claude Bernard in 1851 upon the anatomy and physiology of the sympathetic nervous system. The first was started by the report of Jonnisco in 1896 of his treatment for epilepsy by cervical sympathectomy. During the next ten years a great variety of affections of the head and neck, exopthalmic goitre, tic doloureux, migraine, and glaucoma were treated by excision of the cervical sympathetic chain. But this procedure was soon abandoned as clinical evidence of its lack of therapeutic value piled up.

Then there was a lull in interest in the autonomic nervous system, broken in 1915 by Leriche reporting the results of his periarterial sympathectomies for vascular lesions of the extremities and in 1921 by Jonnisco reporting the relief of two cases of typical angina pectoris by cervical sympathectomies. But it was only after 1924 that these ripples changed to the waves of interest, research and enthusiasm which are now threatening to inundate us. For it was in that year that Hunter and Royle gave their reports on the treatment of muscle spasticity by ramisection.

Since then much work has been done on many conditions supposed to be due to a malfunctioning of the autonomic nervous system, and a voluminous literature has already sprung up. Here in Toronto the first work was done in the Hospital for Sick Children.

Types of Operations.

Surgery of the Autonomic Nervous System can be divided into three procedures. First, there is Periarterial Sympathectomy, which consists in stripping off a collar of the sympathetic network lying in the adventitia of an artery. A modification of this is the infiltration of the adventitia with alcohol.

Next, there is Ramisection, which consists in cutting the rami communicantes as they leave the intervertebral foramina to join the paravertebral sympathetic chain. Royle has popuarized this method.

Finally there is Ganglionectomy, which consists in extirpating certain ganglia of the sympathetic chain, with the intervening trunks. This procedure would seem to be the most effective for the total interruption of sympathetic impulses.

With the actual technique of the operations we need not much concern ourselves. Bearing in mind the anatomy of the paravertebral chains we see

that there are two methods of approach in the lumbar and cervical regions—an anterior and posterior. The posterior is more used and would seem to be the one of choice.

Royle's lumbar ramisection could be counted on to block the sympathetic pathway to the legs, but this method of cutting the rami of the stellate ganglion was not so uniformly certain to cut off the impulses to the upper limb. The reason for this became evident when it was shown that the second dorsal ganglion frequently sends an important ramus to the lower cord of the brachial plexus. This cannot well be reached by a cervical approach. However by a posterior incision, and removing a small piece of the second rib subperiosteally, and then wiping the pleura away from the borders of the two upper thoracic vertebrae the first and second dorsal ganglia can be extirpated and so the sympathetic leak to the upper extremity is intercepted.

Effects of Surgery on Circulation.

The therapeutic possibilities of sympathectomy in circulatory disorders depend upon the conclusion that most of the vasoconstrictor fibres of the part are thrown out of action by the operation. So much blood reaches the region because of the resultant dilatation which is due partly to the unopposed action of the vasodilators and partly to the hemostatic pressure.

Periarterial sympathectomy was the first type of operation to be performed for vasomotor disturbances. A great mass of literature, both pro and con, has grown up since Leriche modified and popularized Jaboulay's operation. The exact manner in which it works is still uncertain. First there is an initial spasm, which is followed by a dilatation. This is short-lived—less than thirty days — according to Leriche and Fontaine.

In many conditions this temporary increase in circulation may be sufficient to produce a permanent improvement, as in healing a stubborn ulcer of the leg, especially if the area is adequately skin-grafted. Also, in passing, one might point out that one of the most valuable points in favor of the operation is its effect in relieving pain in threatening gangrene of the foot, a result whch is obtained in the majority of cases.

Sampson-Handly modified the procedure by injecting 1 to 2 c.c. of 95 per cent. alcohol into the adventitia of the artery. He claims that in addition to being easier and simpler, there is not the initial constriction of the artery that occurs when a periarterial sympathectomy is done.

After the removal of the second, third and fourth lumbar ganglia, with the intervening trunks there is a well-marked vasodilatation in the feet and lower limbs, with a consequent rise in skin temperature, increased heat radiation and visible capillary filling. This lasts at least three years. At the same time there is a loss of reflex sweating, and pilomotor mechanism in the same area.

When the inferior cervical and first and second thoracic ganglia are excised there results a vaso-dilatation of the vessels of the hands and lower arms with a loss of reflex sweating and pilomotor response comparable to that of the lower limbs after lumbar ganglionectomy. The same thing happens on the side of the face, giving a flushed dry skin, and in addition a pseudoptosis, some degree of enopthalmos, and a contracted pupil on that side. These face changes go under the name of a Bernard-Horner Syndrome, and are a constant finding after a cervical ganglionectomy.

Obviously in an ischemia caused by an obliterating endarteritis one would not expect such a brilliant surgical result as in an ischemia due to vasoconstrictor spasm alone. So it is necessary for the surgeon to be able to estimate the ability of the vessels to dilate. One method of doing this is to give the patient a spinal anaesthetic. Providing the anaesthesia includes one-third lum-

bar to the second dorsal nerves the sympathetic overflow is all cut off giving the same result as a lumbar and dorso-cervical ganglionectomy.

Another procedure depends on the relatively certain knowledge that the peripheral vascoconstrictor mechanism is temporarily abolished during a foreign protein reaction, thus also giving the effects of a sympathectomy. Brown and Adson at Rochester in 1929 were the first to utilize this fact as a therapeutic test for the probable efficacy of surgery. The technique of the test is as follows:

An intravenous injection is given of one hundred million dead typhoid-paratyphoid bacilli. The resultant changes in temperature of the mouth and of the skin surface of the extremity in question are determined as accurately as possible, using the centigrade calibration. These values are then applied to the following formula to give what they have named the Vasomotor Index. Vasomotor Index:

(Change in skin temp. minus change in mouth temp.) ÷ change in mouth temp.

For example, suppose the skin temperature of the extremity in question rises 8 deg. C. while the mouth temperature rises 1.2 deg. C. Then the vasomotor index is $(8-1.2) \div 1.2 = 5.7$. These workers claim that, if a patient has a vasomotor index of five or over, sympathectomy should give complete relief of ischemic symptoms, and in all cases with indices of two or more some relief may be expected. So they sum up the question of operation by stating that "after due consideration of the clinical asepect of the case we have advised operation arbitrarily in subjects who have a vasomotor index of two or more.

In order to do away with the very severe reactions which may follow the use of the typhoid injection a more recent modification consists in the substitution for the typhoid of 50 to 100 mgm. of aceto-choline-hydrobromide injected intramuscularly. It must be administered intramuscularly because of its toxic effect if injected directly into the blood stream. Spurling, of Lousiville, speaks very highly of this test, and believes it should be performed on every patient with vascular disease of the extremities before sympathectomy is contemplated. He cites two cases of Raynaud's disease on whom acetocholine was used, and on whom he afterwards operated. He found that the surface temperature following the use of the drug corresponded exactly to the more permanent effects produced by sympathetic ganglionectomy. He also is strongly in favor of using the drug therapeutically, giving repeated injections in the cases, in which, for one reason or another, surgery could not be used.

Raynaud's Disease.

This condition is generally considered to be due to excessive activity or tonus of the vasoconstrictor mechanism,resulting in persistent or intermittent ischemia of the extremities. So it was quite natural that this disease should have been the first of the peripheral vascular disturbances to be attacked by surgery

Recently Thomas Lewis has expressed the opinion that the cause of the arterial spasm is not sympathetic hypertonus, but due to a local process in the walls of the arteries themselves. But be the cause of the underlying pathological process what it may, it is now recognized that this condition gives the most brilliant surgical results of any of the procedures carried out for vascular disease

At first this disease was treated by periarterial sympathectomy, popularized by Leriche. However, finding that some cases resist this treatment he used ramisection. Now the most common operation is lumbar and cervico-dorsal ramisection or better still ganglionectomy. It is only fair to state, however, that some workers think ganglionectomy too radical for milder cases and

do periarterial sympathectomies or repeated protein shocks.

Brown and Adson in 1925 were the first to report a case successfully treated by cervico-dorsal and lumbar ganglionectomy. At the end of three and a half years they reported that the relief from symptoms was complete. These workers have made detailed studies on other patients treated in this manner and report that in these cases they find:

1. Abolition of sweating and pilomotor reaction extending to thighs and axillae.

2. Ratio of arteriole lumen to wall increases from 2 to 1 to 3.5 to 1.

3. Histological studies show an atrophy of disease in the muscular coat of the arteries.

4. Temperature studies show a slight variation due to a vasomotor activity after operation which can occur as a result of local tone of the vessels.

5. Calorimetric studies show a greatly increased heat radiation, often as much as 300 per cent.

Immediately following the operation there are acute changes for some days, detectable as reddening of skin, and an objective and subjective feeling of warmth. This gradually becomes less noticeable, but often as long as three and a half years the extremity so treated is warmer than its fellow.

Many workers have obtained equally satisfying results, so we may consider Raynaud's disease of the extremities to be a controllable malady, if treated by the destruction of the main vasoconstrictor supply to the vessels of the extremities.

Thrombo-Angiitis Obliterans.

It would seem that, in Buerger's disease, in addition to the obliterating endarteritis occluding the main blood channels there are varying degrees of vasospasm, probably in the collateral circulation of the extremity. The etiology of this spasm is obscure but we may hazard the suggestion that the inflammatory process in main vessels initiates afferent impulses, which centrally are relayed back again as constrictor impulses to the vessels forming the collateral circulation of the part. So it is analagous somewhat to the sensory-motor reflex by which an intra-abdominal inflammatory process causes rigidity of the abdominal muscles.

That vasospasm really is present in the diseased extremities is shown by the use of a protein shock, the aceto-choline reaction or spinal anaethesia. It is on this that the rationale of surgery depends, and the more accompanying spasm the better the anticipated results. It is obvious that an accurate determination of the vasomotor index is the sole guide to the proper selection of cases for operation Unfortunately, the percentage of patients with an index of five or over is very small, by the time they present themselves for treatment, and so the complete relief of symptoms is not to be expected. But in many the surgeon can expect a considerable increase in surface temperature, a partial or complete disappearance of cyanosis and pallor, a healing of ulcers, and a marked relief from pain.

In passing it is well to remark that this is a condition where one is wise to consider the therapeutic use of repeated protein shocks or their equivalent. Whether treated by ganglionectomy or by shock, some writer claim that the relief is only palliative, and the disease process in the vessel walls is not arrested. Other workers think, that because Buerger's disease appears to be a self-limiting disease in so many cases, proper therapeutics will tide the patient over the danger period, and so give a permanent cure.

Arthritis.

Rowntree and Adson as early as 1927 reported a case of what they called polyarthritis of the extremities, which was successfully treated by sympathetic gangionectomy. The clinical picture of pallid, cold, painful extremities led them to believe that operation would give relief. Their hope was realized, for

the pallor disappeared, the limbs became warm, the pain vanished and as a secondary change the soft tissue swellings about the joints decreased a great deal. Since then other workers have also reported success with similar treatment.

In 1929 the two workers mentioned above reported on a small series of young patients with severe rheumatoid arthritis on whom they had done dorsal and lumbar gangionectomies. All the patients selected showed a marked improvement following the operation. The secret of this promising form of treatment probaby lies in the selection of cases on which to operate. In order to be eligible for operation a patient should fulfil the following requirements:

1. The arthritis be periarticular with no bone involvement except atrophy.
2. Vasoconstriction be present, causing a cold clammy extremity.
3. Vasospasm be relieved by a test protein shock or some substitute, as spinal anaethesia
4. Patients should be under forty-five and have been given a thorough trial on medical and orthopedic measures.

In addition to surgery being used as a treatment for rheumatoid arthritis it may also be used in certain cases of traumatic arthritis. Leriche has shown that patients with traumatic arthritis often exhibit a remarkable recovery from a chronic state of vasomotor spasm, edema, decalcification, and pain in the injured joint after periarterial sympathectomy or ramisection.

Scleroderma.

Three workers at the Mayo Clinic in 1929 pointed out that a third of patients with scleroderma have associated vasomotor spasm, and that these give fairly satisfactory surgical results. Thye conclude that ganglionectomy or ramisection should be undertaken before fibrosis and atrophy have taken place, for in many of the less marked cases the results were excellent. The advanced cases also were benefitted to the extent of showing a cessation of vasomotor spasm with some warming of the diseased parts, ulcers healing and pain considerably relieved.

Other circulatory disturbances as cold extremities and chilblains have been benefitted by sympathectomies. No reports of surgery done for these conditions alone were found in the literature, but many investigators mention the beneficial results of sympathetic surgery when these were found as a complicating or concomitant feature in the picture.

Effects of Surgery on Pain.

Our knowledge of the pathways of pain transmission over the autonomic nervous system is far from complete. This accounts for the inconstant beneficial effects from operations aimed at the abolition of pain. Of one thing we are almost certain, that the vagi carry no pain fibres.

Pain from Abdominal Viscera.

Some encouraging results have been obtained from the dorsal section of regional sympathetic rami as they enter the intercostal nerves. A preliminary paravertebral novocaine injection in each case should be done to show which rami it will be necessary to cut.

Several writers among them Leriche and Fontaine, have reported successful results from the operation for painful gastric crises in tabes dorsalis. Every other conceivable operation, including extensive section of the posterior roots, cordotomy, and cutting the vagi, has been tried and has usually failed.

For pelvic visceral pain, some successes have been reported by the same writers, who have resected the presacral nerves. Such conditions were treated as idiopathic dysmenorrhoea, irritable conditions of the bladder, and malignancy of the prostrate.

Pain from the Thoracic Viscera.

The important consideration here is angina pectoris and much work has been done on this problem. Whether or

not an operative procedure that relieves the pain of angina is a desirable thing in that it destroys the danger signal of an already damaged heart, need not enter into this discussion. We shall confine ourselves to briefly outline surgical measures for the relief of the anginal pain.

At present one of three surgical procedures is usually tried. The first is the removal of the inferior cervical and first and second dorsal ganglia with the intervening trunks. This is a modification of the original Jonnisco operation and is quite an extensive and difficult one.

The second, or Coffey-Brown, operation is the removal of the superior cervical ganglia with section of the superior cardiac nerves. This procedure is more empirical than based on our knowledge of the cardiac nerve supply. But strangely enough the clinical results are just about as good as the first operation, and it is a much simpler one to perform.

A third and still more simple method has been proposed and successfully executed by White of Boston. He uses a bilateral paravertebral injection of 5 c.c. of alcohol around the first to fifth thoracic sympathetic ganglia. The procedure must be nicely carried out, and the relief varies from a matter of days to at least two years. Since the majority of patients are already victims of advanced heart disease it is obvious that the simplest procedure which will give relief is the most desirable one. So it is wise to keep this method in mind if one is contemplating a procedure to relieve original pain.

Pain from carcinoma of the lung and pleurae and from tuberculous adhesions is transmitted over the upper dorsal sympathetic trunks and has been successfully interrupted by Swetlow and Weingarten by similar paravertebral alcohol injections.

One must think of the possible detrimental effects upon the heart and circulatory apparatus following surgical interference for pain or vascular diseases. We might expect some injury due to—

1. Partial destruction of the nervous acceleration pathways which run to the heart via the upper dorsal ganglia.

2. Marked increase in the size of the peripheral vascular bed.

Brown and Adson intensively studied some cases following cervico-dorsal ganglionectomy. They found that the accelator mechanism is maintained though perhaps diminished in degree. This has been substantiated by other workers. Also the patients respond to exercise subjectively as well after as before operation, while the blood pressure and pulse rate both resting and following exertion behaves within the normal physiological limits. The cardiac output studied before and after operation for Raynaud's disease shows that the load on the heart is lessened as much as 50 per cent.

So although our methods of estimation are inexact and the results difficult to explain with our present knowledge, it seems fairly certain that no danger of cardiac failure exists as a result of interrupting the antonomic accelerator impulses, or of locally increasing the calibre of the vascular bed.

Pain from the Extremities.

Nearly all the work in this field has been done by Leriche. He has shown that, in many cases of ischemic causalgia and amputation stump neuralgias, the pain travels over sympathetic fibres and enters the spinal cord by way of the rami communicantes. In a considerable number of cases he has relieved the pain by ramisection or periarterial sympathectomy, when amputations, sections of the sensory nerve trunks, and even section of all the posterior roots which carry skin sensations from the extremity, have failed.

Effect on Gastric Secretion.

Experiments have shown that, in dogs, section of the vagi above the diaphragm produces a marked reduction of both free and combined HCl; per-

haps because all the so-called psychic stimulation of secretion is removed. When the section is below the diaphragm the free HCl may rise as high as before but the secretory curve is shorter and the stomach empties in about half the time.

C. H. Mayo in a small series of cases of duodenal ulcer has cut all the nerve branches visible while performing a gastro-enterostomy, and has been satisfied with the result. He finds the acids to be lowered by from 25 to 35 per cent.

Effect of Megacolon.

While doing ramisection of spasticity of the lower limbs, Royle noted that one of his cases who had a dilated colon had this lower bowel condition very much improved by the operation.

The rationale of the operation is that, by the removal of the second, third and fourth lumbar sympathetic ganglia with the intervening trunks, the inhibitory sympathetic stimulation to the musculature of the colon and rectum is abolished.

Wade of Sydney, Australia, was the first to apply this operation to Hirschsprung's disease. Judd and Adson were next to report two cases cured by surgery.

These results have been reduplicated by many others. Here in Toronto, the first cases were treated surgically in the Hospital for Sick Children.

Effect of Surgery on Spastic Conditions

In reading over the literature on this subject one becomes confused, and comes to the conclusion that as yet the importance of surgery for spastic paralysis has not been fully determined.

Before the advent of autonomic surgery two operations had been done. Firstly, there was the section of the dorsal roots in selected cases hoping to reduce the hypertonus of the muscles by breaking the reflex arc. Secondly, fasciculectomy, or partial excision of the nerve trunk to the spastic muscles, was tried in order to reduce the innervation and so bring about a balance of antagonizing muscle. Neither operation offered a satisfactory solution.

Then Royle and Hunter appeared with their operation of ramisection followed by the more radical procedure of ganglionectomy and excision of the intervening sympathetic trunks advocated by Brown and Adson. But it must be admitted that the bulk of physiological evidence is against a direct influence of the autonomic nervous system in the maintenance of muscle tone. According to Forbes there is no foundation for the view that the sympathetic nervous system controls a plastic element distinct from the contracted.

Experimentally sympathetic fibres when stimulated do not cause contraction; when cut tone is not abolished.

On the other hand clinically there would appear to be some support for the idea that ramisection or ganglionectomy lessens spasticity. Certainly the circulation of the extremity is greatly improved.

Brown and Adson have concluded from the study of a large number of cases that it is possible to reduce the spasticity of lower extremities in patients with central diplegias, but little or no relief is obtained in apoplexy or the spasticity resulting from diseases or injuries of the spinal cord. Also operation is not indicated in Parkinson's disease for, although it may possibly reduce the spasticity somewhat the tremor and course of the disease is not altered. These writers recommend the operation only in a rather select group of birth injuries, who are free from athetosis and ataxia, and who must be of normal mentality so that they will co-operate intelligently in the process of re-education.

So we conclude in the light of experience of the last few years that the most important effect of the splendid work of Hunter and Royle was the stimulation it gave to investigation of the autonomic nervous system, rather than its therapeutic value in the treat-

ment of spastic paralysis. The arguments for surgery are clinical or empirical rather than based on our known physiology. It is possible that sympathectomy may produce a definite effect by improving circulation and metabolic processes in the spastic muscles. These extremities frequently show marked improvement of circulation and patients usually are grateful to have them lose their cold clammy feeling, even if there is no other improvement. It is therefore desirable to continue the use of surgery in selected cases until a large enough series of failures or successes have been reported to reach a universal agreement.

Because of lack of space, the references are omitted, but they may be had from the author.

Summary.

1. Surgery of the autonomic nervous system is one of the newest forms of treatment for formerly hopeless diseases.

2. In the absence of exact physiological knowledge, much of the surgery is empirical.

3. The most promising results have been for certain circulatory conditions, notably Raynaud's disease.

4. Much more work must be done on this subject before one can arrive at a final conclusion as to its therapeutic value in any pathological condition.

The Symptom—Diarrhoea.

By TREVOR OWEN, M.B., M.R.C.P.

To the layman, diarrhoea may mean anything from sprue, or an acute gastro-entero-colitis with numerous stools. to a frequent or a persistent desire to empty the rectum, due to the irritation of a fissure-in-ano, for example — whether any evacuation takes place or not. It is, therefore, essential to ascertain what he really means by the term.

In considering this symptom, one must keep in mind the complex "mechanism" which governs the motility of the gastrointestinal system, so far as we know it, and eliminate one by one each particular factor, abnormalities of which alter the muscular action in such a way as to produce frequent evacuation. Briefly, and in a general way, normal activity depends on: (1) a normal nervous control, (2) a balanced flow of normal blood and lymph, (3) contents having a normal physical and chemical nature and suitable for that particular organism, and (4) a healthy wall (a) mucous mebrane, (b) muscular coat and (c) peritoneum. Any alteration in one or more of these factors may produce abnormal motility of the whole or a part of the tract.

Diarrhoea from Altered Nervous Control.

No organic spinal nervous disease, of itself, causes diarrhoea. The intestinal tract is supplied by the splanchnic nervous system, a complex of spinal and sympathetic fibres. Of diseases of this "system" almost nothing is known, yet quite conceivably lesions there would disturb the motility of the tract. So far, diarrhoea of this origin has not been diagnosed.

At either end of the intestinal tract this involuntary nervous control is replaced or augmented by voluntary nervous control, so that diseases of the motor and sensory tracts of the latter will alter the control of the rectal sphincter. In motor and sensory lesions, there will be incontinence of faeces which might be complained of by the patient as "diarrhoea." In Tabes Dorsalis the so-called rectal "crises" occur. There is an intense desire to empty rec-

tum but the patient is unable to do so.

A few cases of chronic intermittent diarrhoea are probably due to abnormal function of the vaso-motor system ascribable in some manner to toxaemia from a low grade infection. An increased excretion of water into the intestine with hyperperistalsis leads to evacuation of watery stools. A similar "mechanism" may also be responsible for periodic diarrhoea occurring in migrainous patients.

Among the vaso-motor phenomena can be placed the diarrhoea experienced uring excitement, fright, fear and from exposure to severe cold. These conditions have, however, not been proved to be of this nature, but may rather be due to a transitory physiological hyperadrenalism or hyperthyreoidism, or both.

Certain drugs acting on the nerve endings produce hyperactivity of the gut (e. g. physostigmine).

In the so-called functional diseases of the nervous system diarrhoea may occur. The actual mechanism of its production, whether by abnormality in the nervous impulses or secondary to alteration in the secretion of the digestive juices, is not understood. In hysteria, diarrhoea is not uncommon. Mucous colitis is classed by some as a functional nervous derangement, in which diarrhoea may alternate with constipation with the passage of large or small quantities of mucus not containing pus or blood.

Diarrhoea Due to Vascular Disease.

A. **Arterial**: In the arteriosclerotic, a chronic diarrhoea may be present, but is far more rare a symptom than is constipation.

Embolism: The mesenteric arteries constitute one of the rarer sites for embolism. The interference with the blood supply leads to oedema of the part with haemorrhage and an early symptom is transitory diarrhoea with free blood in the discharges.

Thrombosis of an artery is accompanied by great shock which depends on the size of the branch affected as also does the occurrence of diarrhoea with bloody stools; the larger the artery the less likely is it to be a symptom because of the death of a section of bowel, leading to symptoms of intestinal obstruction.

B. **Venous**: Thrombosis of the mesenteric veins occurs secondarily to portal thrombosis or to compression by enlarged mesenteric glands, pancreatic or gastric tumours, or by local peritonitis due to gall bladder disease or peptic ulcers. Primary thrombosis occurs in the branches of veins from any ulcerated or inflamed area in the bowel, especially in the terminal ileum, appendix or caecum. In pylephlebitis, the diarrhoea may be paroxysmal. Diarrhoea is a symptom in about 50 per cent. of the cases of venous thrombosis. The onset is characteristically sudden with severe generalized colicky pain and if diarrhoea occurs, the stools are bloody. Constipation and symptoms of intestinal obstruction follow.

Passive congestion from myocardial failure, if severe, and especially if of long duration, causes diarrhoea probably from oedema of the intestinal walls.

Diarrhoea from Obstruction of Lymph Flow.

In obliterative lesions of the retroperitoneal lymph glands (e. g. Tabes mesenterica) the absorption of fat may be completely prevented and produce a chronic diarrhoea. The same phenomena may occur in obstruction of the thoracic duct.

Diarrhoea Dut to Changes in the Quality of the Blood.

Alteration of the haemoglobin content or in the number of red and white cells does not, in itself, account for the symptom of diarrhoea occurring in such cases. In the leukaemias, infiltration of the wall and particularly of the lymphoid tissue by the abnormal leuco-

cytes may provoke reaction in the wall as in any other new growth. In methaemoglobinaemia and sulphaemoglobinaemia, a chronic diarrhoea is often associated. It is to abnormalities of the plasma that this heading refers. All forms of toxaemia, organic and inorganic, and exogenous or endogenous in origin, are included in this group. The intestinal tract is a pathway for the excretion of all toxins and therefore those of all acute infections (e. g. diphtheria, bacillary dysentery, cholera, etc.), inorganic poisons (e. g. mercury, arsenic), organic endogenous toxins (e. g. renal insufficiency, liver insufficiency, acute gout); all may produce diarrhoea by injury to the wall when concentration is great. This is an added factor in those diseases (e. g. bacillary dysentery) where the primary lesion also is in the intestinal tract. The diarrhoea of hyperthyroidism is probably a direct action on the muscle from an increased "thyroxin" content of the blood.

Diarrhoea Due to Abnormal Quality of the Contents.

Mineral oil in excess and laxative or purgative substances can be mentioned under this heading, though some not strictly so. The absence of bile in obstructive jaundice and of the pancreatic secretion in obstruction to the pancreatic duct gives rise to incomplete digestion of fats, and the irritation due to fatty acids may cause diarrhoea. Achylia gastrica is frequently the apparent factor in a form of looseness of the bowels taking place after any food.

In some individuals diarrhoea is an allergic phenomenon after partaking of certain foods. Egg, milk and shellfish are the most common. While nearly all persons of this nature are early aware of their peculiarity, the presence of the harmful ingredient may not be apparent in the dish eaten.

The toxins of deteriorated or infected foods, spoken of under the name "ptomaines," are also not an infrequent cause of local epidemic diarrhoea.

Diarrhoea from Diseases of the Wall of the Intestinal Tract.

Infections specifically attacking the intestinal wall cause hyperperistalsis by inflammatory reaction with or without ulceration, and have diarrhoea as one of the chief symptoms. It is not the purpose here to describe the clinical characteristics of these diseases (amoebic and bacillary dysentery, tuberculosis and syphilis of the intestine, typhoid and paratyphoid fever, ulcerative colitis, cholera, fungus infections, leprosy).

Inflammatory or degenerative changes not due primarily to infection are seen in pernicious anaemia, pellagra, sprue, amyloid disease, scurvy.

New growths, polyposis, diverticula (the appendix is a diverticulum) and peritoneal disease, cause diarrhoea either by mechanical irritation or by ulceration and secondary infection, or by haemorrhage. It is often of an intermittent type.

Symptoms Indicating the Part of the Tract Infected.

The higher up in the gut the abnormalty is, the more will the diarrhoea be related to, or exaggerated by, the taking of food (e. g. achylia gastrica), or be accompanied by vomiting or nausea (e. g. acute enteritis).

Hyperperistalsis of the small bowel, if severe, produces a generalized colic with sharp "narrow" pains.

When the colon is affected there is little or no change in relation to taking food. Colic, if present, is felt as a "broad" pain more likely to be localized than that arising from the small intestine. There may be regional tenderness.

As the site of the lesion approaches the rectum, tenesmus becomes a more prominent symptom. Naturally, if the whole tract, from stomach to rectum,

is involved, all these symptoms may be present together.

The Information Gained from Examination of the Stools.

(a) Regarding the Position of the Lesion. Watery stools arise in the small intestine. Bright red blood is usually from the sigmoid colon, or rectum, and the nearer the lesion is to the ileocaecal valve the darker red will the blood be. Blood from the small intestine is changed still more and that coming from the duodenum is tarry.

Large amounts of mucus probably indicate the small bowel, and small amounts the colon, as being the affected part.

Very acid, sour smelling, light coloured and "crumbly" stools are associated with small intestinal lesions due to abnormalities in the digestive processes.

Undigested food particles, especially meat, are present in small intestinal diarrhoea (lienteric diarrhoea).

Very small discharges indicate a rectal lesion.

A long period of constipation followed by the evacuation of enormous stools is pathognomonic of Hirschsprung's disease (megacolon).

(b) Regarding the Kind of Lesion.

Pus means ulceration.

Blood cells mean congestion, but gross blood means ulceration or simple rupture of a vessel, purpura, thrombosis, embolism, or new growth.

The specific organism can often be found at the proper time in tuberculosis, bacillary and amoebic dysentery, typhoid and paratyphoid fever, in parasitic infestations and the fungous infections.

An attempt has been made to consider the question of diarrhoea as an example of the method which should be and can be employed in working out the origin of each symptom of any symptom-complex. The omission of any, or a change in the order, of the various steps will often result in a general sense of bewilderment. The investigation of "diarrhoea" will emphasize the fact that short cuts to diagnosis are short cuts to failure.

The Learning of Anatomy

By PROFESSOR J. C. B. GRANT.

Your representative has paid me—a recent intrusion into the Medical Faculty—the compliment of asking me to make some contribution to your journal; a journal which is the envy of and a stimulus to many an undergraduate body. It was his particular request that I should say something about the Teaching of Anatomy. With this, in a manner, I comply, wondering, however, why his request was not rather that some remarks be made on the Learning of Anatomy, and hoping that it was because he appreciated that learning and teaching are often one and the same, for after all, is not the best way to learn by teaching? For this remark I have the high authority of one who was a professor of chemistry, a physician, a liguist and much more. His reply to a Chinese student, who went to study at a certain university and who inquired of him if he would assist him to find someone willing to instruct him in the English language, was "What you want is not a tutor in English, but a pupil." This epigrammatic remark is not without depth; it is applicable to the study of anatomy. Though it is true that every student in a class can hardly expect to be officially recognized as a member of the teaching staff, neverthe-

less unofficially each student is or should be a teacher — teaching others and teaching himself — giving and receiving private tuition.

In learning anatomy as in teaching the subject we must above all else endeavour not to depend upon our memories, because our memories will fail us, but upon an understanding and appreciation of a region or structure. There are those who say that knowing anatomy is merely evidence of a good memory; and that to remember it you must read your anatomy books at least once a year; but this is not true.

We are discussing just now the learning of anatomy by undergraduate medical students. It is understood that the requirements of the artist, the nurse, the student of pure science, the student of medicine, the masseur and the instructor in gymnastics are in the matter of anatomy all different. Their purposes and reasons for desiring to acquire a knowledge of the subject are as diverse as are the uses to which they propose subsequently to put their knowledge. Economic reasons may perhaps require these groups with diverse aims to study together; but no other reasons dictate this procedure.

To those who propose to follow the calling of a physician or a surgeon it is descriptive anatomy that is of primary importance. The learning and teaching of descriptive anatomy is apt to be looked upon as dry and uninteresting and as imposing an unholy tax on the memory; and, if this branch of anatomy is studied solely as one might study the plan of some town that grew up in total disregard of any system of town planning the subject can become as unattractive and desolate as is such a town early of a Sunday morning. If, on the other hand, it is studied and considered with some regard to general principles, the functions of parts embryology, morphology, applied anatomy, experimental anatomy, evolution, history of anatomy, the subject will appear to bristle with interest. Important details and relationships, once so mastered, will always remain within certain recall.

In my hope that the foregoing remarks will not be regarded as vague abstractions and insincere generalities —and what are more distasteful than empty platitudes? — I supply a few concrete examples, which, if you will consider them, may render my meaning more clear.

A house surgeon once meeting me in a hospital greeted me with a statement and a question. The statement was to the effect that he had just examined in the outpatient department a man who had severed the tendon of his middle finger, and that he proposed to suture the ends together. The question he put was "How far do the fleshy fibres of the entensor muscle of the middle finger extend and at what level exactly does its tendon begin?" Now, a glance at the dorsum of one's own hand, when the fingers and wrist are fully flexed, reveals the fact that the muscles of the back of the forearm pass over an extensive convexity which begins at the lower expanded end of the radius and ends at the tips of the fingers. It is a principle that the highly specialized fleshy fibres of a muscle, when subjected to a pressure ample enough to impair seriously their blood supply, always give place to fibrous tissue (tendon or aponeurosis) which is relatively a nonvascular tissue. From this it follows that the muscles on the dorsum of the forearm must become tendinous from the point at which they first touch bone, in this case from about half an inch above the wrist joint, and that they remain fibrous from there onwards to their insertions. It is also a principle that under such circumstances a lubricating device, a bursa or bursae, will be found to intervene between the tendons and the site of friction. Bursae must, therefore, occur in front of the extensor tendons. Now from a glance at the back of one's own wrist, when dorsiflexed or hyperextended it is clear

that the tendons of the extensors are prevented from taking a straight course (the course a bowstring would take) by the restraining influence of the dorsal carpal ligament. A site of pressure, therefore, exists behind the tendons as well as in front of them; from which it follows that bursae are required behind the tendons as well as in front of them; the bursae will not be circular, but elongated. If these anterior and posterior elongated bursae become one, a synovial sheath results. Synovial sheaths extend from about an inch above to about an inch below the point at which their tendons are subjected to pressure. If you appreciate and consider these remarks it becomes unnecessary to remember how far above the wrist and the ankle the various muscles become tendinous or to remember the extent of their synovial sheaths.

Again: it is not strictly correct to say that the great trochanter of the femur is subcutaneous, because in truth it is covered by the Gluteus Maximus. But, when the Gluteus Maximus crosses the great trochanter it is subjected to severe pressure and, therefore, in obedience to the law, its substance becomes fibrous or aponeurotic; and, between this aponeurosis and the bone in order to reduce friction a bursa, the trochanteric bursa, makes its appearance. The trochanter, therefore, is not merely subcutaneous but it is also subaponeurotic.

The easiest and most certain method of finding the deep surface of the Gluteus Maximus is to cut right down through the skin and gluteal aponeurosis till the great trochanter is encountered, then to pass a finger through the incision and sweep it around between the Maximus, which alone will be superficial, and deeper muscles.

The degree of pressure exerted by one fleshy muscle on another is presumably never sufficient to necessitate the presence of a bursa. Loose areolar tissue appears to be satisfactory intermuscular lubricant, and if the subject is obese the areolar tissue, here as elsewhere, may become converted into adipose tissue. If two muscles, such as the Glutei Medius et Minimus, arise and are inserted close together, if the fibres of one are parallel to the fibres of the other and if they contract together. then for practical purposes they are one muscle with two names; and as there is no play between them there is no call for areolar tissue between them. The origin and insertion of the Gluteus Maximus are not near those of the Medius and Minimus. The actions of this muscle are, in fact, antagonistic to those of the Medius and Minimus, its shape is different, and its fibres play across those of the Medius and Minimus. This being so, in order to afford the Maximus freedom of action it is obvious that an appreciable quantity of areolar tissue must intervene between it and the deeper structures. The surgeon, operating in this region, will know that he has cut completely the Maximus when this necessary layer of areolar (perhaps fatty) tissue accosts him.

The longitudinal and circular muscle coats of the intestine play at right angles to each other. Surely areolar tissue will be found between these coats. It is because loose areolar tissue occurs deep to the circular fibres of the External Sphincter Ani that the surgeon is enabled to separate this muscle from the underlying longitudinally directed fibres of the Levator Ani.

If a student of pure science were asked the direction of the fibres of the Internal Oblique and Transverse muscles of the abdomen, the answer "Those of the former passed upwards and medially; those of the latter horizontally," might be regarded as satisfactory, because in so far as the upper four-fifths of their fibres are concerned this is true. But from the point of view of the medical student the answer is inadequate, because the statement is not true of those fibres of the internal oblique and transversus which lie be-

low the level of the anterior superior iliac spine and these, surgically and medically, are the most important fibres these two muscles possess. These portions of the two muscles arise from Poupart's Inguinal ligament, lie parallel to each other, and arch downwards and medially to end in the conjoined tendon and for practical purposes are one muscle. Hence, their importance to the medical student.

If the foregoing remarks are appreciated no difficulty will be found in replying to the query: "Is a layer of areolar tissue to be found between both the upper and lower parts of these two muscles?"

Make observations on yourself. Do not consult a textbook to discover if rotation can take place at the knee joint, but with your leg hanging over the arm of a chair satisfy yourself by palpation that as you turn your foot medially and laterally the tibia does rotate on the femur. When fully extended no rotation can take place; the joint is rigid.

The above is explained by the fact that the collateral ligaments of the knee joint are attached not to the centres of the sides of the condyles of the femur but eccentrically to the posterior parts of the sides of the condyles; in fact, to the epicondyles. Hence, they are slack when the joint is flexed; taut when it is extended. This appreciated, it is an easy matter to run the fingers along the course of the collateral ligaments, which, when examining the knee, you may wish to do. Owing to a similar eccentric attachment of the collateral ligaments of the metacarpophalangeal joints the fingers can be abducted and adducted when the joints are extended, but not when flexed.

It is evident that in man the fibula does not help to support the weight of the body. What then are its uses? (a) to give origin to muscles, (b) to keep the talus in position, and (c) to act as a pulley for the Peronei Longus et Brevis. As only one muscle, the Biceps, is inserted into the fibula and as eight muscles take origin from it and pass downwards to the foot, it follows that unless some structure or structures, in addition to the Biceps, resist the downward pull of these eight, the fibula will turn from its moorings when these muscles are in action. The additional resisting structure is the interosseous membrane. If it has such an office to perform there is only one direction its fibres can usefully take; that is downwards and laterally. To prevent lateral dislocation of the talus the interosseous membrane must be exceptionally well developed and strong in the region of the lateral malleolus. Here, in fact, the membrane does become expanded and is known as the interosseous ligament, the anterior and posterior fibres of which are referred to as the anterior and posterior tibiomalleolar ligaments.

In association with this it may be noted that the bird has no separate tarsus; neither has its fibula a lower end. The upper half of the fibula alone exists and is utilized for muscle attachments. In the horse the body of the fibula is missing. Its lower end is small and fuses with the tibia. Its talus is in part kept in position by an anteroposterial ridge which descending from the tibia, fits into a corresponding groove on the upper aspect of the talus and plays the part of an accessory or intermediate malleolus. In man this groove may be detected but it is so wide and shallow as to have no restraining value and the presence of a shaft to the fibula is evidently necessary to stabilize his malleolus. In man the fibula malleolus may be felt to be triangular and to descend lower than the tibial malleolus. It, therefore, articulates with a larger area on the lateral side of the talus than does the tibia on the medial side. It descends so low, in fact, that it covers the whole depth of the lateral surface of the talus which is therefore completely occupied by a triangular facet. The tibial melleolus can create but a small facet on the upper part of

the medial surface of the talus; the rest of the surface being rough for the deltoid ligament. That is to say, the strength of the ankle joint depends laterally on the bone only; medially, partly on the bone but largely on ligament. To tell which side a talus belongs the above facts have but to be appreciated and considered. To learn them would be foolish.

A complete palate is peculiar to mammals. Man is a mammal. The very term implies that in infancy he must have lips with which to grasp a nipple, otherwise he could not suck. Equally, he must have an extensive hard and soft palate in order that the nasal pharynx may be shut off from the mouth when sucking. With the appearance of this palate new muscles are not called into being, pre-existing ones are modified. These may be derived either from the immediate neighbourhood or from a distance. Muscles may as it were be native or immigrant. Most of the muscles of the soft palate are to be regarded as natives—as belonging to the same group as the superior constrictor of the pharynx, for they have the same nerve supply, the accessory nerve. One, however, the Tensor Palati, derives its nerve supply from the Trigeminal nerve, via the otic ganglion. It is an immigrant.

The actions of the two muscles, the Levator Palati and Tensor Palati are revealed in their names. But, as they arise side by side, from the base of the skull, one would expect that they would both elevate the palate. It is because the Tensor makes a recurrent course around the hamulus of the medial pterygoid process that it is enabled to render the palate tense (and slightly to depress it). The answer to the question "Where is the hamulus"? may be inferred from the foregoing remark. It must lie below the level of the hard palate otherwise the Tensor will act as an elevator, and as the medial pterygoid process forms part of the lateral wall of the nose, it must be in the plane of the medial wall of the nose, from which it follows that it can be palpated from the mouth just below and behind the hard palate. And, of course, the Tensor must become tendinous and must possess a bursa where it makes the turn.

Let these few examples serve to illustrate the contention of my theme. To a teacher what could be more distressing than to find a pupil removing areolar tissue with no more thought than he would give to the brushing away of snow from his path, not tracing tendons to their insertions, ignoring the attachment of ligaments, cleaning muscles, vessels, nerves, conscious only of their names and endeavouring to commit to memory the words he reads. And, to the pupil how unattractive and monotonous is such work and how hopeless it must seem. Let him acquire a certain inquisitiveness. Let him ask himself questions; say to himself, "Why is the posterior border of the ulna sharp and the anterior border rounded," or conversely let him put the question, "what will be the appearances of the posterior and anterior borders of the ulna if the deep fascia and the aponeuroses of the Flexor Carpi Ulnaris and Extensor Carpi Ulnaris are all three attached to the former, and the fleshy fibres of the Flexor Profundus Digitorum to the latter?" "Is it safer to work on the medial or lateral side of the great sciatic nerve?" or conversely, "Do the ham muscles, which the sciatic nerve supplies, lie to its medial or lateral side?" For in this lies the answer to the question. "Why are there sesamoid bones in some tendons and not in others?" "Do sesamoid bones lie in front of joints or in contact with the ends of bones?" "Could a sesamoid bone occur in the tendon of the Subscapularis?" "Why do the upper fibres of the deep fascia of the front of the leg take a vertical course and those of the lower part a circular course?" "How do you know that the temporal muscle must have a tendon on its lateral surface, the Psoas on its

postero-lateral surface and the anterior crural muscles on their lateral sides?" "If the femoral artery, vein and lymphatics have each a separate sheath, why has the nerve no sheath at all?"

When he gives thought to his work, then will he find a meaning and an interest in it also and what he learns in this manner he will not readily forget.

Then will he become not only a pupil but a tutor also to himself.

Those interested in this method of approach may find further articles by myself in

1. The Canadian Med. Association Journal, 1925, xv., pp. 1195-1201.

2. Bulletin of the Association of American Medical Colleges, Jan., 1928, Vol. 3, No. 1, p. 1.

Malignant Disease of the Female Genital Tract.

By W. G. COSBIE, M.B.

There is no need to emphasize the importance of the study of malignant disease of the female genital tract. In adult females one death in twelve is due to cancer and nearly one-third of these are growths originating in the uterus.

Of late years three factors have stimulated our interest as gynaecologists in the study of cancer. First, the advent of radium with a gradually perfecting technique has brought a hope of cure and prolongation of life to many otherwise doomed. Secondly, more detailed study of the histological features of the disease has given us more definite ground for the basis of our prognosis. Third, the development of Social Service work has made it possible to keep in touch with our cases and so develop statistics which are of real value.

Although the cause of cancer is unknown, still a brief consideration of some modern conceptions is not lacking in value. There appear to be two causitive factors, first, an inherent predisposition or susceptibility on the part of some somatic cells to undergo dedifferentiation toward the embryonic type. How much heredity has to do with this is not settled but the work of Maud Slye with mice is very convincing. The age incidence of certain carcinomata might suggest an endocrine imbalance with the freeing of energy or growth previously expended in work. Secondly, there is the exciting factor, the irritant which, whether it be parasitic, diatetic, bio-chemical or traumatic, is an essential to the development of malignant growth.

Mayo has said: "I have never observed a case of cancer in which there has not been some pre-existing instability of the tissues and a long continued irritation. It would seem as if the long suffering tissues respond to the chronic insult of the injury by supplying repair cells less and less mature until finally through sheer inability to supply sound cells to heal the lesion, the tissues reach a stage in which there is an uncontrolled production of unsound cells too immature to heal the breach of continuity or furnish surface protection to normally protected tissues."

Carcinoma of the Cervix.

Carcinoma of the cervix stands second only to carcinoma of the breast as a cause of female deaths from malignancy. The striking facts with regard to its occurrence are: First, that 95 per cent. of those suffering from this growth have been pregnant and that multiparity is of great importance. Second, that the occurrence of cervical laceration with cervical catarrh or erosion or chronic endocervicitis is undeniably recognized as the predisposing

state to the later development of cancer. In the nulliparous, chronic infection and developmental abnormalities, e.g., erosions or stenoses are important aetiologically.

A short consideration of the histology of cervical erosion is very enlightening. The parturient injury may be considered as a traumatic ulcer, which soon becomes infected. Of the two types of epithelium adjacent, the columnar, gland-bearing epithelium shows more rapid growth and gradually extends downward to cover the denuded area. Slowly and in the absence of marked infection and heavy discharge, the squamous epithelium gradually undermines and replaces the surface covering of columnar epithelium. Certain factors which delay the healing process have been noted, namely, infection if deep seated stimulates overgrowth of glandular tissue within the cervical canal as well as on the portio vaginalis and the excessive mucous discharge resulting not only tends to maintain the columnar epithelium but by maceration drives back the growth of squamous epithelium. So that there is an ebb and flow of either type of epithelium and with constant irritation of both — a stimulus to more active growth, of cells less and less mature. The hypothesis is not far to seek.

The histologic nature of cervical cancer has been extensively studied of late. The squamous-celled or epidermoid and the columnar-celled or as it is generally recognized, adeno-carcinoma, are well recognized types. From 87 per cent. to 95 per cent. belong to the former group. The work of Schottlander, Martzloff, and Broders has resulted in assigning various degrees of malignancy to three subdivisions of epidermoid carcinoma, the ripe, mid-ripe or unripe tumours, depending on the predominant cell type.

1. Ripe or prickle-celled with cells simulating in appearance the superficial layers of the epithelium.

2. Mid-ripe or transitional celled, with cells simulating the mid portion of the epithelium.

3. Unripe or spindle-celled or sometimes called basal-celled cancer composed of young cells rapidly reproducing and simulating embryonal tissue.

It is to be noted that these types are not held to originate from these three layers and for the present we shall be content to state that the index of malignancy increases as the cell type becomes less mature.

The gross clinical appearance of cervical cancer is well known to all of you, affecting primarily either the portio vaginalis or the endocervix—and tending to extend principally, by outward proliferation or by infiltration. The tumour is cauliflower or ulcerative in type. The pathognomic symptom of irregular bleeding results from erosion and sloughing of the hard friable mass. At its earliest manifestation simply a small hard nodule of the cervix which tends to project as a sloughing mass with induration of the vaginal walls and neighboring cellular tissues and body of the uterus. Finally the erosion is extreme—the cervix disappearing and the vault presenting a crateriform ulcer, the bladder and bowel may be involved and fistulae develop.

Glandular involvement affecting primarily the iliac group is common, but metastases are comparatively rare. In a larger series of autopsies only about 40% showed this complication.

The ureters are often compressed in extensive growths, so that it is not surprising that urinary tract sequelae terminate many cases.

The extent of growth is very important in determining the nature of treatment and estimating the hope of cure. The American College of Surgeons has adopted the following classification.

Class A—confined to the cervix.

Class B—with extension to the body of the uterus or to the vaginia.

Class C—extension into the cellular tissue.

Class D—the "frozen pelvis"—bladder rectum and glandular involvement.

There are certain further factors of prognostic value to be considered:

(a) The amount of stroma appears to make some difference, especially where radium is used in treatment. Theoretically, radium is most effective in scirrhus types of growth because part of its effect results from stimulation of connective tissue.

(b) The majority of patients are between 35 and 50 years of age. It has been demonstrated that patients under 40 and over 65 years of age respond poorly to treatment.

(c) The hope for the cancer sufferer is early diagnosis. In the spindle and transitional cell types of growth a duration of symptoms for eight months puts the patient beyond the hope of an operative cure. Spindle cell growths develop more rapidly and adeno-carcinoma more slowly.

The diagnosis of carcinoma of the cervix is suggested by the occurrence of irregular bleeding but it cannot be too strongly emphasized that the growth has attained appreciable size before bleeding will occur. Bleeding will occur in cancer beginning within the cervical canal because it is not exposed to trauma.

Recognizing the fact that most often cancer develops in the cervix, the site of chronic cervicitis, one must examine such cases carefully. Profuse leucorrhoea is distinctly pathological and any area of hardness in the cervix, especially if there is spotting of blood on examination, should cause suspicion.

The careful examination of removed tissue in case of cervical repair and the use of biopsy, will establish what might otherwise be obscure. It is very rare indeed to discover cancer where it is not suspected, but many a suspicious case is diagnosed for certainty and many a woman is freed from suspicion.

The Treatment of Carcinoma of the Cervix.

The treatment of carcinoma of the cervix may be said to begin with prophylaxis. There is no need to go further than quote the statistics of the Free Hospital for Women that in 5,962 cases operated upon for chronic disease by trachelorrhaphy, amputation or cautery, only 5 have been known to develop cancer, and these were all cervical repairs; and figures published by Levin in the J.A.M.A., who found in 613 cases of cancer only two women who had previous cervical repair. Routine post partem treatment of the lacerated and catarrhal cervix is now pretty generally advocated. Light cauterization results in rapid epithelialization.

Up to fifteen years ago the recognized treatment of cervical cancer was radical extirpation. Prior to 1878 cancer had only been treated palliatively by curetting or the cautery. But in this year hysterectomy by the abdominal and the vaginal routes was introduced by Freund and Czerny respectively. The name of Wertheim will always be remembered because his method standardized Pan-hysterectomy and was accepted by the profession of the world. Continental and British surgeons have shown remarkable results from extirpation. With the advent of radium the tendency has been away from radical surgery with its high immediate mortality, until at the present time, in America at least surgical extirpation is practically relegated to the realm of history.

The season for this change is best exemplified by the figures of Heyman of Radiumhemet, Stockholm.

1. The absolute cure rate of carcinoma of the cervix.

Surgical Treatment. (Literature of the World)	Radium. Radiumhemet 14-23
Cases, 5,806	790
Cured, 1,111	163
Absolute cures, 19.1	20.6
Average operability %, 54.6	25.5

Bacterial Endocarditis

By J. A. DAUPHINEE, M.D.

In this thesis it is proposed to discuss the condition of bacterial or infective endocarditis with special consideration of the subacute type. Some of the aspects of the bacteriology, exciting and predisposing causes, and pathology of the disease will be presented. The clinical picture and the diagnosis will only be considered in so far as they arise in the discussion of the pathology.

A concise description of the disease is given by Horder (1920) as follows: "Subacute Bacterial Endocarditis is then the accepted name of the condition having more or less the following features. The onset is most often insidious, the general symptoms include loss of strength and tone. A sallow complexion with anaemia, a moderate loss of weight, and fever. The heart gives evidence of endocarditis at some time or other in all cases and in the majority there has been previous valve injury. Widespread arterial embolism takes place. In most cases there is a positive blood culture, sometimes a short streptococcus, much less often Pfeiffer's bacillus, always an organism of low pathogenicity. The course of the disease is slow but progressive and though remissions may recur it is, once established, almost invariably fatal. The total duration is from three months to two years with an average of six months. Death occurs from toxaemia, from heart failure, from uraemia, or from cerebral or coronary emboli. The post mortem findings include a vegetative endocarditis on the valves or wall of the heart with little or no ulceration and widespread infarcts without suppuration. As a result of the embolic processes there is found a form of glomerular nephritis more or less characteristic of the disease."

The condition of subacute bacterial endocarditis is of much interest not only because of the protean nature of its symptoms, of its very grave prognosis, but also because of its close and important relationship to the most important of all heart diseases, namely, rhenmatic fever. The history in these cases of an antecedent rheumatism or chorea is so frequent that it has been dwelt upon by everyone who has written about the disease. The relationship is so marked that it may be said that the one main predisposing factor in the production of subacute bacterial endocarditis is rheumatic fever; and one might even go so far as to say that a superimposed bacterial inflammation may be considered as a complication of a rheumatic endocarditis.

BACTERIOLOGY.

A. The Organisms Concerned.

The valves of the heart may be infected with any of a large number of different organisms. Thayer (1926) in a monumental monograph on the subject of "Bacterial (infective) endocarditis." gives tables of the aetiological organisms in his series of 198 cases and tables showing the duration of the condition when caused by different organisms.

These data, as well as those compiled by Blumer (1923) for 304 cases, may be summarized as follows:

(1) Streptococci were the etiological factor in 70 per cent. of cases, or 56 to 80 per cent.

(2) Pneumococci, staphylococci, and gonococci were about equally responsible for the remaining 30 per cent. of cases.

(3) Other organisms, such as Pfeiffer's bacillus, staphylococcus albus, Bacillus pyocyaneus, Bacillus anthracis, Meningococcus, Micrococci, were the etiological factor in rare cases.

(4) The duration of Streptococcal endocarditis was mainly over two

months. This was true in two out of every three cases.

(5) The duration of endocarditis due to other cocci was under two months in all but a few cases.

In this regard Blumer states, "There are only two organisms concerned with subacute bacterial endocarditis in the great majority of cases, the so-called streptococcus viridans which causes most of the cases, 95 per cent. according to Libman's extensive studies, and the Bacillus Influenza which causes the remaining 5 per cent." This is in agreement with the opinion of other workers who have investigated the organisms which are responsible for subacute bacterial endocarditis.

B. Blood Culture Results.

Widely divergent conclusions are reported as to the results of blood cultures in bacterial endocarditis. Horder (1908-9) obtained positive findings in about 90 per cent. of his cases, but in a later series (1926) reported only 47 per cent. positive. Wright (1925) obtained positive results in 63 per cent. of cases but his review of blood culture findings by American, German, English and French investigators shows figures ranging from 6 to 100 per cent.

Libman (1923) states that a positive culture of anhaemolytic streptococci does not necessarily mean a bacterial endocarditis. Such a result may be associated with:

(1) Cases of subacute bacterial endocarditis.

(2) Cases of rheumatic fever and chorea.

(3) Mixed cases of these two.

(4) Invasion of the blood stream from active or quiescent focal infections especially tonsils.

(5) Invasions from acute inflammatory conditions, such as thrombosis of lateral sinus, post partum infections, etc.

(6) Secondary or terminal invasion in a variety of conditions.

(7) A curious group of cases described by Oille, Graham and Detweiler which were characterized by sub-febrile temperature and the presence of anhaemolytic streptococci in the blood stream—23 cases and all recovered.

Thus it is seen that positive blood cultures are not necessary to make a diagnosis of bacterial endocarditis and also that a positive blood culture in the absence of other signs of the disease does not mean a bacterial involvement of the heart valves.

C. The Streptococcus Associated with Subacute Bacterial Endocarditis.

According to Libman and Aller (1910) the cocci found in cases of subacute and chronic infective endocarditis are all gram positive. They have never been found to have a capsule. They are either round, ovoid, or lancet shaped and may be found as diplococci or in chains. Every organism except one was found sooner or later to grow in chains which were often very long and convoulted. They are usually smaller than the ordinary streptococcus or pneumococcus and grow more poorly. They are non-haemolytic, and are insoluble in bile. The organisms are as a rule not very pathogenic for animals.

Wright (1925) found that the action of these organisms on carbohydrates varied with the different strains but was constant for all strains isolated from the same case. He found the group to be quite heterogeneous serologically although some degrees of inter-relationship could be demonstrated between individual strains by agglutination tests and to a more marked degree by means of complement fixation. He agrees with Libman in respect to their low virulence for laboratory animals.

AETIOLOGY.

Under this heading there will be considered very briefly the probable source of the organisms which cause a bacterial endocarditis to develop in an individual. Though the condition can frequently be traced to a source in the case of acute types associated with virulent organisms the reverse is true in

the case of the more chronic forms and in many cases the probable source of the infection can not be demonstrated.

On the other hand, organisms probably get into the blood stream of everybody upon occasion. Are there any factors which might increase the ease with which such organisms may invade the heart valves? Are there any conditions under which ordinary foci of infection may liberate more than an occasional organism into the general circulation? What effect has previous disease? What has the relationship of a general or localized decrease in resistance got to do with the onset of bacterial endocarditis? These questions may be considered under the heading of predisposing causes.

A. Exciting Causes.

A summary of cases investigated by Thayer (1926) and Blumer (1923) indicates:

(1) That the probable source of infection in subacute bacterial endocarditis was uncertain in 70 to 80 per cent. of cases whereas in acute bacterial endocarditis the source of infection was uncertain in 40 per cent. of cases.

(2) That where the source of infection was practically certain the portals of entry were acute respiratory infections. upper respiratory infections, and infections of the female generative organs in 80 per cent. of cases.

Horder (1926) is sceptical about the relationship of such foci of infection and states, "But between the very common finding of salivary streptococci in apical tooth abscesses and the relatively uncommon finding of salivary streptococci in the endocardium, there is a wide gulf to bridge. With the whole alimentary tract teeming with streptococci of this and allied types, it is quite a question if the area of focal sepsis is more than an epiphenomenon in the process of deep seated infection."

B. Predisposing Causes.

(a) Age: All agree that death from acute rheumatic disease occurs most frequently in the first two decades of life. While death from the late results of acute rheumatic heart disease is common in middle life, the great majority of fatal cases of acute and subacute rheumatic heart disease occur in youth.

Subacute bacterial endocarditis is uncommon in children but most common in young adults. The investigations of Rost and Fischer (1928) and Blumer (1926) show that about 50 per cent. of these cases occur between 10 and 30 years of age. The second decade represents the maximum period of incidence for subacute bacterial endocarditis as it does also for gonococcal endocarditis (70 per cent. according to Thayer, 1926). Pneumococcal endocarditis is a disease of middle and late adult life whereas staphylococcal endocarditis occurs with more or less equal frequency throughout life.

(b) Sex: Most investigators find a preponderance of incidence in males though the actual ratios are not definite.

(c) Congenital Cardiac Defects: From an analysis of 555 cases Abbott concludes that infective endocarditis is extremely common in patients with cardiac defects who live to maturity; that the process when it involves anomalies of the left heart is most commonly of the subacute type, whereas in septal defects and patent ductus an acute infection is relatively more frequent and here the lesion is usually right sided. Lewis and Grant (1923) found that 23 per cent. of patients with congenital bicuspid aortic valves who reached adult life developed an infective endocarditis of the aortic valves. Wauchope (1929) found that less than 5 per cent. of congenital bicuspid valves developed infective endocarditis.

In general, most investigators agree that congenital cardiac defects definitely predispose to infective endocarditis and that in order that such cases live to maturity that these cardiac defects are of the milder types, e.g., patent ductus arteriosus.

(d) Acquired Valvular Defects.

Rheumatic Fever. That bacterial endocarditis is frequenty superimposed on valves already scarred by previous disease has long been recognized. Thayer's analysis shows that the order of frequency of pre-existing valvular disease in bacterial endocarditis is Gonococcal, Pneumococcol, Staphylococcal, Acute streptococcal, and Subacute streptococcal. The figures of Horder, (1908-09). Clawson (1924). Wauchope (1929), and Thayer (1926) show that pre-existing valvular disease occurred in from 56 to 80 per cent. of all cases of subacute bacterial endocarditis.

(e) Strain. War Service: In the series of endocarditis in soldiers reported by Coombs (1922-23), Starling (1922-23), Murray and Lougheed (1921), Wauchope (1929), there was a very noticeable lack of a history of rheumatism or of previous valvular disease. The disease also differed in attacking the aortic rather than the mitral valve and was more chronic than reported by other workers in civilians. According to Coombs the disease attacked almost without exception men of fine physique and morals, who joined the army early, and who exerted themselves to their utmost. Murray and Lougheed also feel that strain plays a part in the localization of the disease on the aortic valves.

PATHOLOGY.

The pathological lesions which result from and characterize a bacterial endocarditis are readily understood when one considers the nature of the process. In these cases there is as stated before an inflammation of the valve cusps, chiefly mitral and aortic, by organisms, in some cases virulent, in other cases of very low pathogenicity. This inflammation results in the growth of thrombotic vegetations on the valves, which are readily broken off and discharged into the blood stream. Here, then, we have a definite cardiac lesion, which continually discharges microorganisms and emboli into the main arterial stream. The three headings therefore under which we may discuss the pathology of the condition are:

(a) Cardiac Lesions.
(b) Septicaemia and Toxaemia.
(c) Embolic phenomena.

Cardiac Lesions.

The lesions in the heart in bacterial endocarditis, as opposed to those of rheumatic fever where the whole structure of the heart is involved, are more or less limited to the endocardium, a fact which has led Horder (1926) to propose the name "endocarditis vera" for this condition. Blumer (1923) points out that the cardiac lesions of subacute bacterial endocarditis present three outstanding features, namely:

(1) Implication of valves already damaged by previous endocarditis.

(2) Involvement of the mural endocardium and chordae tendinae.

(3) Relatively slight involvement of myocardium.

Many cases enjoy complete cardiac sufficiency for months after they fall victim to the infection. The time that will elapse before cardiac failure ensues will depend to a large extent on the condition of the myocardium before the onset of the valvular infection. As bacteria frequently attack valves already damaged by disease, however, cardiac failure may appear early. Figures diverge fairly widely as to the frequency of terminal heart failure. Horder (1926) found it in 40-50 per cent. of his cases. Clawson (1924) found that 82 per cent. of his cases of subacute bacterial endocarditis showed oedema or fluid in the cavities. The incidence of heart failure, however, was much less in the cases of secondary acute endocarditis, whereas in the primary group cardiac failure again predominated.

Myocardium: Such lesions as do result in the cardiac muscle itself from the infection are obviously embolic (Coombe, 1920). In the acute forms an acute suppurative focal myocarditis may occur bringing forth a polymorphonuclear response. In the case of sub-

acute bacterial endocarditis one finds, according to Libman (1923), an essentially round cell interstitial lesion, the so-called Bracht-Walchter bodies. These lesions are not present in all cases and are not specific. Clawson (1924) found that only a few hearts from subacute bacterial endocarditis cases showed Aschoff bodies (6 cases out of 54, all with a history of rheumatic fever) whereas he found this typical lesion in 8 out of 9 cases dying from acute rheumatism.

Various combinations of cardiac hypertrophy and dilatation are seen and the usual changes associated with mitral or aortic lesions occur. Blumer (1923) noted "very slight hypertrophy" in 6 out of 84 autopsies and "no enlargement of heart at all in an equal proportion." Wauchope (1929) reports hypertrophy of cardiac muscle to be constant and that microscopical myocardial lesions are not uncommon in endocarditis lenta. She also noted infarcts or areas of fibrosis in 31 of 131 cases. Wright (1925) states that bacteria may sometimes be demonstrated in the heart muscle capillaries but with no accompanying evidence of inflammatory exudate.

Pericardium. That the frequency of paricarditis in acute rheumtic fever is much greater than in subacute bacterial endocarditis has been emphasized by numerous workers. Clawson and Bell (1926) found pericarditis in 72 per cent. of 18 cases of acute rheumatic fever coming to autopsy and only in 22.5 per cent. of cases of subacute bacterial endocarditis. Pericarditis is relatively infrequent in bacterial endocarditis, acute or subacute, except when it is caused by a preceding attack of acute rheumatic fever.

Endocardium. The Valves Involved. Clawson (1924) investigated the valves involved in acute rheumatic fever, primary and secondary acute bacterial endocarditis, and subacute bacterial endocarditis. He found:

(1) That the mitral valve was involved in close to 80 per cent. of all these cases,

(2) That the aortic valve was involved in from 30 to 70 per cent. of all these cases,

(3) That the tricuspid valve was involved in about 55 per cent. of cases of rheumatic fever but rarely in other forms of endocarditis.

(4) That the mitral and aortic valves were involved at the same time in 25 per cent. of cases of subacute endocarditis but rarely in other forms.

(5) That the wall of the heart was attacked in about 20 per cent. of cases of subacute bacterial endocarditis but rarely in other forms.

(6) That ulceration occurred in about 25 per cent. of cases other than those of rheumatic fever from which there was no ulceration.

Blumer (1923) found that about 40 per cent. of cases of subacute bacterial endocarditis showed involvement of the mitral valve alone, and about 40 per cent. showed involvement of both the mitral and aortic valves.

Thayer (1926) found that staphylococcal infections attacked the aortic and mitral valves about equally in 60 per cent. of cases: that gonococcus, however, attacked the aortic valve by preference, there being 66 per cent. aortic lesions, and only 19 mitral lesions in his series: and that pneumococcus attacked the aortic cusps in 50 per cent. and the mitral valve in 30 per cent. of cases.

It would appear then, that bacterial invasion of valves occurs far more frequently on the left side of the heart than on the right. Of the valves on the left side the mitral valve appears to be involved much more often than the aortic in the subacute types of endocarditis. In the case of returned soldiers with endocarditis, however, (Coombe, 1922-23; Starling, 1922-23; Murray and Lougheed, 1921) the aortic valve seems to have been involved almost to the exclusion of the mitral (11 aortic to 2 mitral in 15 autopsies, Coombs). In the acute cases the mitral valve les-

ions also preponderate but to a less extent than in the more prolonged cases. The gonococcus seems to have a decided predilection for the aortic valve.

Involvement of the mural endocardium is fairly characteristic of the subacute form but it may be present in the acute cases. Horder (1920) mentions one case in which bacterial vegetations of endocardium were entirely mural, the valve cusps being quite unaffected. He found mural involvement in 52 per cent. of 118 post mortems. Thayer, (1926) reports as high as 84 per cent. involvement of the mural endocardium in chronic cases. The auricular infection is more common than the ventricular.

Mechanism of Invasion of Valves.

The actual method by which the organisms become lodged in or on the valve is still undecided. The organisms may reach the valves by one of two paths: either by way of the coronary circulation, or by way of the general blood stream bathing their cusps. Osler (1885) thought that from the position of the early vegetations and from the fact that colonies of micrococci can be seen directly on the endocardium that the latter was the correct view. Murray and Lougheed (1921) are of the opinion from India ink injection experiments that the main portion of the valves are avascular. They note, too, that the line of closure around the corpora auranti is not perfectly smooth but is slightly corrugated and that, after the India ink has been washed away by a stream of water so that the endocardium is perfectly clear, this line of closure is marked out under the microscope by minute granules of the ink adhering to these irregularities. They think, therefore, that organisms are deposited on the heart valves at the line of closure in the same way as are these particles. According to Horder (1926) Carey Coombs has quite recently convinced himself that whereas the rheumatic virus reaches the cusps and produces a valvulitis from within these structures, the bacteria in septic endocarditis attack the valves from the blood circulating around the cusps.

On the other hand Luschka (1852) (quoted from Kerr and Mettier, 1925-26), claimed that normal valves have blood vessels to the line of closure. Bayne-Jones (1917) has shown by injecting the coronary arteries with a mass of carmine and gelatine at 45 deg. C. under a pressure of 140-190 mm. of mercury for 30 minutes that the atrio-ventricular and semilunar valves and chordae tendinae of the pig are well supplied with vessels which differed only in numbers from those in the human heart. He describes a hedge like plexus in the semilunar valves occupying about one-half of the membranous portion. No vessels were shown in the thin portions of the valve cusps or in the nodules aurantii. Kerr and Mettier (1925-26) injected the coronary arteries of the pig's heart with a mixture of India ink diluted with an equal volume of distilled water under a pressure of 150-200 mm. of mercury. After the pressure had been maintained for about a minute the heart was fixed in formalin. In their experiments the vessels were shown to extend in the atrio-ventricular valve leaflet beyond the line of closure and to be continuous with vessels along the chordae tendinae to the papillary muscles. The semilunar valves were more difficult to inject. They suggest that their results point to an invasion of the valve in bacterial endocarditis through the coronary system by way of the small vessels in the valve substance which they describe.

McCallum (1928) states that blood vessels run far in towards the periphery of the atrio-ventricular valves but enter only a short way into the bases of the semilunar valve. He suggests that since bacteria are found first lodged on the face of the valve along the line of closure that the organisms are somehow caught there from the blood stream as the valves beat together. According to him, it is difficult to understand why the organisms should so frequently select the line of

closure of the mitral valve and leave the rest of the endocardium free, if they come in by way of the coronary circulation. He also points out that Grant (1924) has shown in many cases of endocarditis that, when bacteria have lodged on a valve and eroded it so that it flaps about new implantations occur on whatever part of the heart lining the flapping valve strikes against and nowhere else. Horder (1926) is of the opinion that we still lack evidence that is conclusive.

Certainly it would appear that scarred valves are less resistant to bacterial infection than normal ones but whether the organisms reach the valves through their own circulation or through the blood bathing their surface still remains to be decided.

The Valvular Lesions. (Osler, 1885; Libman, 1923; Wright, 1925; Clawson, 1924). (a) Macroscopic. In acute rheumatic endocarditis the valves show small smooth globular nodules at the points of contact of the leaflets. These little graular excrescences lie parallel to, but back from, the free border of the valve and in acute rheumatic fever they generally remain in this line. These heal by scarring and ultimately result in stenoses and insufficiencies.

In acute bacterial endocarditis there are fibrinous deposits first found being the lines of contact of the leaflets. These may spread and grow. Abscesses and ulcerations of the valve may occur and there may be definite perforations of the valve cusps. The vegetations that form may be quite small or quite large, red, soft and velvety in appearance. They are structurally similar to those of the subacute variety.

The chief lesions found on the valves in the more chronic cases of infective endocarditis occur in the form of soft villous vegetations. They are usually large, pedunculated, though sometimes sessile, and cauliflower-like. They are frequently calcified in parts and often almost completely fill the orifices. The consistency and size of these vegetations makes it easily possible for particles to break loose into the blood stream and produce the embolic phenomena so characteristic of the disease. When the mitral valve is involved there is a tendency for the vegetations to spread up on to the left posterior wall of the auricle. Often the chordae tendinae attached to the posterior flap are covered to a greater or less extent by vegetations. Nearly always the anterior flap is also involved. Not uncommonly the chordae are ruptured, the torn ends at times being massed together by vegetations at the edge of the flap. The vegetations are yellowish, greenish, pinkish or reddish in color and vary much in size in different cases. When the condition is prolonged, changes in the direction of organization may be seen. Fibroid induration may take place in the deeper parts while the superficial portion remains unchanged and necrotic. Not infrequently the deposits are gritty from the deposit of lime salts. There is little tendency to ulceration and if ulceration does occur it is usually in the aortic flaps.

In the cases of endocarditis lenta in ex-soldiers (Starling, 1922-23; Coombs, 1922-23) fibrosis and calcareous change in the involved valves was more marked than in the other cases. Ulceration in these cases was rare. The masses of fibrin attached to the valve grew to a remarkable length out of all proportion to the smallness of endocardial inflammation from which they sprang.

(b) Microscopic. In acute bacterial endocarditis the organisms cause a purulent infiltration over a wide area of the valve with resulting necrosis and ulceration. A large thrombotic, blood platelet mass, the vegetation, results This is invaded by the polymorphonuclear leucocytes and by such numbers of organisms that there is a veritable row of colonies on the surface of the vegetation. Organization occurs in the deeper layers in patients who do not die within the first few weeks.

In cases of subacute bacterial endocarditis the primary lesion, though

small, is larger than it is in acute rheumatic fever. There is no purulent inflammation but a proliferative process with a tendency to round cell infiltration. The blood platelet mass that is formed is invaded by large numbers of bacteria forming definite rows of colonies especially near the surface of the mass. The vegetations contain few polymorphs. Occasionally foreign body giant cells are found, constituting when present a characteristic lesion of this type of endocarditis. The freshly formed portions of the vegetations consist almost entirely of bacteria which prevents the adjacent endothelium of the endocardium from spreading over the vegetations. In the deeper and older portions the bacteria tend to disappear and here an active fibroblastic invasion is always to be seen in which lime salts occasionally are deposited (Libman 1923).

Wright (1925) notes that bacteria can very readily be demonstrated in the periphery of the lesions, when taken from cases with a positive blood culture, but that organisms are difficult to find in the deeper portions and that there are none at all in the valve substance itself. The bacteria close to the surface retained the gram stain firmly but the more isolated organisms nearer the cusps tend to be decolorized. In all the sections he examined the absence of polymorphs from the neighborhood of the peripheral bacterial mass was very striking. On the side of the vegetation near the cusp he occasionally observed large mononuclear cells crowded with cocci.

The reaction within the cusps is mainly of a chronic nature, the predominant cells being of the mononuclear type.

In cases of subacute bacterial endocarditis in which the blood culture was negative Wright generally failed to find organisms at all in the valve vegetations. However, he did see in the vegetations masses of granular material situated in a position similar to that occupied by the bacteria in the bacteremic group. Staining reactions convinced him that these masses were streptococcic colonies undergoing a process of degeneration. He failed to observe any similar material or bacteria in any case of endocarditis of a rheumatic type.

Septicaemia and Toxaemia.

The valvular invasion of bacteria by organisms constitutes a seat of acute or chronic infection which is constantly discharging into the blood stream both living bacteria and products of their metabolism. There is set up, then, a fairly constant septicaemia from which on account of the location of the lesion there is no escape without the abolishment of the source which unfortunately only rarely occurs.

With the more virulent organisms which are the causative factors in the acute and fulminating types this is a very serious condition. The organisms are spread in the blood stream and are caught in some part of the peripheral tree where they may produce multiple small suppurative abscesses. The results to the patient are the same as those from any acute suppurative process in which the organisms find their way into the blood stream. There is a profound toxaemia. The fever is high and may be widely fluctuant. Rigors and profuse sweats are relatively common. The white count is very high showing a marked increase in the polymorphonuclear leucocytes—altogether the picture of an acute septic infection.

In the subacute or chronic form the organisms are of extremely low pathogenicity as a general rule. Of the relative frequency of positive blood cultures in such cases, somewhat has already been said. The number of organisms which may be found in the blood stream in the bacteraemic state varies from one or two organisms per 25 cc. of blood, up to as high as 6,500 organisms per 1 cc. The septicaemia in this condition is peculiar in its long persistence and in its absence of suppurative lesions. Here in a mass of thrombus

widely separated from the tissues of the valve and unattacked by the cells of the blood washing the surface of the thrombus, apparently not destroyed by the blood fluids, the organisms multiply and escape into the blood stream. The septicaemia is a secondary phenomenon and is dependent on the egress of organisms from the valve lesions.

The white count is only slightly elevated, averaging 10,800, according to Cotton (1920). Clawson and Bell (1926) state that 39 per cent. only of their cases showed a leucocytosis of over 15,000. Wauchope (1929) reports that a leukopenia is more common than a leucocytosis. This is in marked contrast to the acute form such as that caused by the pneumococcus in which 82 per cent. of cases showed over 20,000 white cells per cubic mm. Horder (1926) gives the average white count in the chronic endocarditis as being 9 000 and in the acute form 22,000.

There may be slight continual fever or febrile periods alternating with exacerbations of pyrexia. There is general malaise, headache, loss of weight, and strength, and a slight anaemia which becomes more marked as time goes on. In Blumer's (1926) series of subacute cases, in which the disease ran a clinically insidious course, the most frequent early complaint was weakness, either alone or accompanied by fever, emaciation, arthralgias, or cardial nervous or digestive disorders. Feebleness, asthenia debility, exhaustion, prostration and malaise were all used to convey this impression. The loss of weight may be slight or extreme. Loss of appetite is of frequent occurrence.

These evidences of septicaemia and toxaemia — those of chronic infection — become more severe as time goes on. The patient becomes pale and frequently assumes a peculiar dirty color—the cafe au lait pigmentation of Libman. Other manifestations of toxaemia probable are enlargement of spleen (partly also due to embolic infarcts) and albuminurea. Toxic swelling of liver and heart may occur. Clubbing of the fingers which occurs frequently may be in part caused by the toxaemia.

Embolic Phenomena.

As has already been stated a number of times, the valvular lesions on account of their frequent location in the left heart and of their friable nature, are prolific sources of arterial emboli. Embolic processes are found in some of their various forms in most cases of the subacute bacterial endocarditis and less frequently in the acute forms—probably because the vegetations tends to be larger in the first mentioned.

Clawson (1924) on the subject of embolic phenomena concludes:

(1) That petechiae occur in all forms of endocarditis, but particularly in subacute bacterial endocarditis.

(2) That petechiae are the only evidence of embolic disturbance to be noted for rheumatic fever.

(3) That the occurrence of infarcts in the spleen and kidney is about 40% of cases and equal for both subacute and acute bacterial endocarditis.

(4) That cerebral embolism occurs in 17% of cases of subacute bacterial endocarditis.

(5) That embolic nephritis is a phenomena particularly associated with subacute bacterial endocarditis and that it is the most frequent and striking evidence of embolism in that condition (55%).

The embolic processes in the subacute type are distinguished by being non-suppurative in contrast to similar lesions of the acute type. Let us consider these embolic processes in greater detail.

Skin.—(a) Petechiae. White topped petechiae are probably evidences of skin emboli. They appear about the clavicles and over the shoulder blades. Other common situations are chest, forearm, legs, and buttocks. They are short lived. They tend to appear in crops. There is no definite proof that they are embolic in origin (Horder 1926). Similar spots may occur in the cornea.

(b) Osler's Nodes. Although Osler himself (1908-9) refers to them as the "nodosite cutanees ephemeres" of the French, they are generally called by his name. They are ephemeral spots of stinging, painful, nodular, erythema chiefly in the skin of the hands and feet. They may have white centres resembling an urticarial wheal. He states that they are not beneath, but are in the skin. The pads of the fingers and toes, the thenar and hypothenar eminences, the sides of the fingers and the skin of the lower part of the arm are the most common localities. The percentage of cases in which they have been found varies greatly, but Blumer (1925-26) states that they can be found in about 40% of cases. This condition is generally supposed to be pathognomonic of the subacute bacterial endocarditis, but Blumer reports seeing it in at least one case of fulminating endocarditis due to Staphylococcus aureus. Deep emboli may lodge in the fingers, giving rise to painful digits without demonstrable swelling.

(c) Splinter haemorrhage. Blumer (1925-26) has also called attention to what he calls splinter haemorrhages. The patient suddenly complains of a sore finger and on examination there is found a linear haemorrhage 4-5 mms. long beneath the nail.

(d) Janeway Lesions. Libman (1906 and 1923) calls attention to what he calls the Janeway lesions which are "small haemorrhages in the palms or soles with slightly nodular character," which in contrast to Osler nodes are not painful or tender. These occur according to Libman almost exclusively in cases of acute bacterial endocarditis.

Spleen.—Splenic enlargement is a usual finding in the subacute type of endocarditis. Starling (1922-23) found enlarged spleen in 80% of one group and in 100% of a second group. Clawson (1924) found spleens of over 200 gms. in weight in 62% of subacute bacterial endocarditis; 49% of secondary acute cases; 71% of primary acute cases and in 33% of acute rheumatic fever cases. Spleens of over 500 gms. were found in 11-14% of the bacterial cases and not at all in the acute rheumatic cases. Infarct of spleen is the most common evidence of arterial embolism at autopsy. Starling (1920) found splenic infarcts in 12 of 17 cases of the subacute bacterial endocarditis coming to autopsy. Clawson found them in 47% of subacute and in 40% of acute cases of the disease.

The spleen at autopsy is described by Wauchope (1929) as being characteristically a chronically inflamed spleen. It is greatly enlarged and firm and shows upon the cut surface trabeculae and enlarged Malpighian bodies. Microscopically, the pulp shows an infiltration of the chronic type, the majority of the infiltrating cells being plasma cells and large mononuclear cells with deeply basophilic cytoplasm. Occasionally, however, in the typically chronic cases a spleen showing little or no enlargement is found at autopsy. It appears that the inflammation and consequent enlargement of the spleen may diminish in the intermissions of bacteremia. In a number of cases pain in the splenic area is followed by a rapid enlargement of the organ and in such, infarcts are found after death. If these events are correlated the enlargement must be due to oedema or inflammation caused by the embolism and not to the infarct itself, which is not larger than the healthy tissue it replaces.

Kidney.—Albuminuria occurs in the majority of cases and miscroscopic or macroscopic blood in the urine can be made out very frequently. Macroscopic blood may be due to infarction of kidney producing a triangular area of necrosis as in spleen. However, there is set up in the kidney of cases of subacute endocarditis a form of focal nephritis which is practically characteristic of the condition. This has been described by Baehr (1912, 1921) and by Gaskell (1911-12) who state that Lohlein was first to describe the lesion in 1910. This is a pathological lesion

which affects one or more loops of a variable number of the glomeruli. The following description is taken almost verbatim from Baehr (1912). The very earliest stage of the process appears to consist of a slight swelling of the glomercular epithelium of the involved loops. This may be situated in any part of the involved tuft. If the lesion is large, a segment of the glomerulus or even the entire Malpighian body may be involved in the process. At first the outlines of the swollen epithelial cells in the diseased segment can be made out. Subsequently these are lost and the entire structure is fused into a homogeneous finely granular material. If this finely granular mass is situated at the periphery of the glomerulus the epithelium of the visceral layer of Bowman's capsule over the involved part is usually found to be swollen, proliferating and desquamating into the capsular space. Eventually this epithelium undergoes necrosis as did previously the swollen epithelium of the involved loop of the glomerulus. It also becomes a part of the homogeneous, finely granular mass, which now fuses with the parietal layer of Bowman's capsule. At this stage, the mass may become flattened out over the area of fusion with Bowman's capsule in a crescentic fashion.

The homogeneous cellular material is seen to be traversed by a very delicate network. Eventually the entire mass becomes thoroughly organized. At the same time there occurs active growth of the epithelial cells of the adjacent intact portions of the parietal layer of Bowman's capsule. They advance over the inner aspect of the necrotic mass which has by this time usually separated somewhat from the rest of the glomerulus. Eventually the entire lateral surfaces of the mass are covered by this invading epithelium.

The healed stage presents the following picture. There is present a hyaline mass having roughly the shape of a truncated pyramid. Its base is fused with the adjacent interstitial tissue; the mesial aspect adherent to the remainder of the glomerulus; its sides clothed by a reflection from the adjacent epithelium of Bowman's capsule.

When the entire glomerulus is involved, the peripheral portion may be seen to be replaced by concentric fibrils of connective tissue, whereas the central portion still consists of homogeneous material. However, the glomerulus may be entirely replaced by a mass of hyaline fibrous tissue.

In individuals dying in the active bacterial stage, all stages of glomerular lesion are found. Typical lesions were found in 23 out of 25 cases. The percentage of glomeruli involved varied from 2-75%. The lesions are characteristic of subacute bacterial endocarditis. Healed lesions were found in the bacteria free cases. No similar lesions at all were found in 54 cases of acute bacterial endocarditis.

(To be continued)

Some Remarks on Duodenal Ulcer.

By E. E. CLEAVER, B.A., M.B.

In general practice, duodenal ulcer is a very common disease. Probably from one to two per cent. of the population suffer with this condition at some time or other during their lives.

Hurst thinks there is a general ulcer diathesis which renders an individual liable to the development of chronic ulcer. Campbell and Conybeare have shown that a large percentage of healthy men have short stomachs, with hyperchlorhydria, hypersecretion, active persistalsis and rapid evacuation. The above conditions although compatible with perfect digestion, are, in the opinion of these observers, essential predis-

posing factors in producing duodenal ulcer. The infective factor in the development of duodenal ulcer has been quite generally emphasized and also the important part played by the gastric juice.

It is my intention in this short paper to emphasize certain features of ulcer that are not often stressed. A large number of cases that present themselves in an office practice are well nourished and healthy individuals, who give no history of any infective process and have no focus of infection that can be demonstrated. Often they are men in business and professional life who live under conditions of physical and nervous strain. Their history is definitely duodenal. Their attacks of pain are generally of short duration and pain during the night is not common. Some of these cases have long periods of entire freedom from symptoms. Investigation is negative except that frequently there is radiological evidence of a spastic duodenal cap. Many of these cases have been followed over long periods and, when adhering to treatment, show no radiological evidence of ulcer. Other cases of the same type, after a period of months or years, in which no supervision or proper treatment has been carried out, show definite radiological evidence of ulcer. This group of cases we designate as duodenal spasm. They may be regarded as potential ulcers. These cases of duodenal spasm, if under proper supervision and control as to conduct of life, habits and diet, generally do not develop a frank ulcer.

Another type of duodenal spasm is not infrequently seen which is due to a definite extrinsic cause, such as appendicitis, cholecystitis, etc. To cite a typical example: A young man consulted me some years ago on account of attacks of pain which recurred each spring and fall. The picture at once suggested a duodenal ulcer. X-ray investigation showed a duodenal cap with characteristic filling defect, and also a tender, kinked appendix, six or seven inches in length. A second X-ray examination, after administration of 3-100ths of atropic sulphate, showed a normal duodenal bulb. It was only after repeated questionings on several occasions that the history of an acute attack of pain in the right iliac fossa, with vomiting, was obtained. At operation, a pathological appendix with adhesions was found and examination of pylorus and duodenal cap showed no evidence of ulcer.

Although pain is present in 90 per cent. of duodenal ulcers, we may have symptoms of discomfort, gas, heartburn, emptiness and rarely nausea, with definite periodicity. To cite an example, a woman of forty consulted me on account of neausea two or three hours after meals. These attacks came in cycles and there were often intervals of months with entire freedom from symptoms. It was suggested to the patient that she try taking food when nausea was present.Relief of this symptom was most marked. The radiological finding was positive for duodenal ulcer. Later, this patient had two severe hemorrhages. Operation was performed and a typical duodenal ulcer found.

Location of pain. In my experience, pain is most frequently located in epigastrium and left hypochondrium. Pain in right hypogastric and right iliac region is not infrequent. Pain in left hypogastric and left iliac region is not unusual. Pain behind sternum is complained of occasionally and strongly suggests to the patient and often to the physician cardiac involvement. Some years ago a man consulted me on account of pain in left lumbar region. He remarked almost shamefacedly that the pain was relieved by taking food.

Gastric analysis in duodenal ulcer without obstruction generally shows a high acid curve, but the most important feature is the consistent presence of free HCl. Personally I have seen only one case of duodenal ulcer with the absence of free HCl. If the clinical

history is typical and the X-ray findings positive, but repeated gastric analyses show an absence of free HC1, I would hesitate to make the diagnosis of duodenal ulcer. On two occasions at the Toronto General Hospital, patients were operated on for supposed duodenal ulcer. At operation, no ulcer was found. In both cases, gastric analysis showed an absence of free HC1.

Haemorrhage. In a series of 190 duodenal ulcers who were seen in an office practice, 16 per cent. gave a history of having had tarry stools on one occasion. Only 3 per cent. gave a history of having repeated haemorrhages, i.e., on two or more occasions. Based on the above findings, operation is advised after a second series of haemorrhages.

Obstruction. Duodenal obstruction practically always demands surgical interference. A patient consulted me on account of marked duodenal obstruction. X-ray examination was positive and there was a large residue at twenty-four hours in the stomach. The patient elected not to have an operation. Gastric lavage was carried out each night for a period of one month. A recheck with the X-ray showed a characteristic duodenal ulcer but no gastric delay. A few cases are seen with marked asthenia. These cases show no evidence of pathology at the pylorus or duodenum but there is often a large gastric residue at 24 hours. The stomach under the fluoroscope is hypotonic and shows very few peristaltic waves. These patients improve on gastric lavage, a dry diet and large doses of tincture of nux vomica with a bitter stomachic.

Treatment. In the treatment of the ambulatory cases, certain features are necessarily emphasized. The patient should be given some idea of the nature of duodenal ulcer and the marked tendency of the ulcer to recur. Foci of infection, such as teeth, tonsils and sinuses, should be attended to. The importance of avoiding worry, excitement, mental and physical strain and fatigue should be stressed. These cases should spend at least nine hours in bed at night and lie down for one hour during the day. Regulation of the bowels is essential and mineral oil is advised. Alcohol and tobacco should be avoided. One of the most important features in treatment is the taking of a glass of milk, buttermilk or one or two biscuits between meals and at bedtime. A general diet is given in which raw fruits and raw vegetables are avoided. It is hardly necessary to emphasize the importance of avoiding condiments, sweets, twice-cooked meats, pastry, etc. This plan is advised for at least six months and at the end of that time the patient is instructed to follow the same regimen for another six months. By the end of a year they have generally learned how to conduct their lives, how to avoid worry, excitement, etc., and have also formed the definite habit of taking something regularly between their meals.

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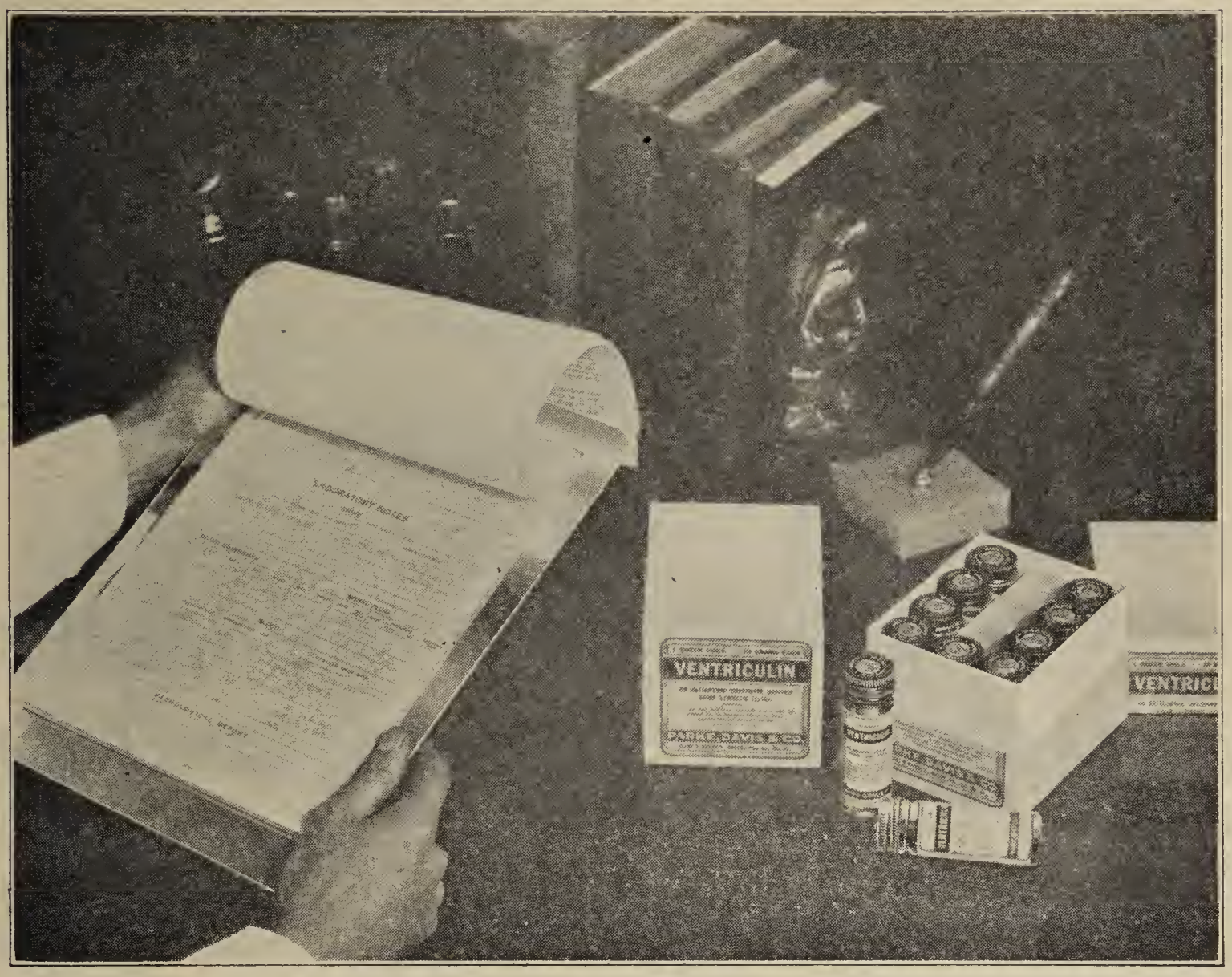

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